

ANOVA of ADHD score for the genotypes of 20 genes

Gene	11	12	22	F-ratio	p	Gene score
	N	Mean	SD	N	Mean	SD
Dopamine genes						
<i>DRD1</i> SNP Ddel						
Lit	39	20.10	10.2	164	17.58	11.1
Optimized						
<i>DRD2</i> SNP Taq IA						
Lit	15	15.93	10.3	120	19.50	10.2
Optimized						
<i>DRD3</i> SNP Nsc1						
Lit	152	17.68	11.2	157	18.34	11.0
Optimized						
<i>DRD4</i> 1' 48 bp repeat						
Lit	56	19.00	10.9	162	17.98	10.5
Optimized						
<i>DRD5</i> 2 dinucleotide repeat						
Lit	74	18.63	11.4	111	19.15	11.3
Optimized						
<i>DAT1</i> 3' repeat						
Lit	21	15.33	12.4	142	17.41	10.9
Optimized						
Serotonin genes						
<i>HTR4</i> 4' (SLC6A4) promoter ins/del						
Lit	85	16.20	10.9	159	19.11	10.9
Optimized						
<i>HTR1A</i> SNP C-1918G						
Ind	82	19.00	10.61	177	17.31	11.4
Optimized						
<i>HTR1B</i> (HTR1DB) SNP G861C						
Lit	202	18.49	10.9	167	17.30	11.1
Optimized						
<i>HTR1DA</i> SNP T1350C						
Ind	266	18.16	11.3	70	19.34	9.7
Optimized						
<i>HTR2A</i> SNP T102C MspI						
Lit	58	17.88	11.2	172	18.59	11.0
Optimized						
<i>TDO2</i> SNP G->A Int 6B5a						
Lit	315	17.98	11.0	17	20.65	10.4
Optimized						
<i>TPH</i> SNP A 779 C						
Lit	60	19.00	10.4	180	17.73	10.8
Optimized						

Figure 1(a)
 (continued)

Gene	11						12						22						F-ratio	p	Gene score
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD			
Neuropeptide genes																					
<i>DBH</i> SNP <i>Taq I</i>																					
Lit																					
Optimized	67	16.81	10.1	168	18.78	11.1	101	16.69	11.3	1285	0.28	220									
<i>ADRA2A</i> SNP promoter region <i>Msp I</i>																					
Ind																					
Optimized	186	17.42	11.1	128	16.8	10.5	22	21.95	11.7	1.96	0.14	012									
<i>ADRA2B</i> del/ins																					
Ind																					
Optimized	155	18.14	11.5	158	16.46	10.6	23	19.73	9.6	0.215	0.81	102									
<i>ADRA2C</i> 6 dinucleotide repeat																					
Ind																					
Optimized	131	18.77	10.5	113	15.79	11.0	92	20.17	11.2	4.45	0.012	102									
<i>NET</i> (<i>SLC6A2</i>) SNP A1970G <i>Man</i>																					
Ind																					
Optimized	155	17.82	11.2	144	19.04	10.6	38	16.6	11.3	0.914	0.402	120									
<i>PNMT</i> SNP G-148A																					
Ind																					
Optimized	110	16.89	11.1	156	19.59	10.9	66	17.58	10.9	2.05	0.129	012									
<i>COMT</i> SNP val 158 met, G1947A, <i>Null</i>																					
Ind																					
Optimized	75	19.42	10.8	175	18.52	11.0	86	16.52	10.8	1.55	0.212	210									

Lit, references for literature-based gene scoring; Ind, gene scoring based on our studies of an independent set of subjects; SNP, single nucleotide polymorphism.

¹ *DRD4*: 11 = any < 4; 12 = 4/4; 22 = any > 4.

² *DRD5*: 11 = 148/148; 12 = het; 22 = non 148/non 148.

³ *DAT*: 11 = non 10/non 10; 12 = 10/non 10; 22 = 10/10.

⁴ *HTT*: 11 = SS; 12 = SL; 22 = LL.

⁵ *HTR1DA*, *TDO2* since there were only 2 22s, they were combined with the 12s.

⁶ *ADRA2C*: 11 = < 183; 12 = het; 22 = 183/183.

ANOVA of ADHD score for the Genotypes of Twenty Genes

Gene	11			12			22			F-ratio	p	Gene
	%	Mean	S.D.	%	Mean	S.D.	%	Mean	S.D.			

Other Neurotransmitter Genes

HTR6 SNP (Shinkai et al. 1998)

ADHD	2.8	12.33	9.7	27.1	18.26	10.3	70.0	18.66	11.2	1.44	.23	012		
ODD		3.0		2.3		3.91	3.1			3.64	3.2	.44	.64	021
CD		2.11		1.5		3.65	2.6			3.17	2.6	2.05	.13	022

GABRB3 dinucleotide repeat (Mutirangura et al. 1992)^a

ADHD	38.0	18.99	10.8	47.9	17.48	11.1	14.1	19.69	10.9	1.05	.35	102		
ODD		3.57		3.1		3.55	3.2			4.47	3.1	1.67	.18	002
CD		3.01		2.2		2.97	2.4			2.91	2.4	.089	.91	200

GABBR1 dinucleotide repeat (unpublished)^b

ADHD	9.5	17.5	11.7	27.0	19.1	11.7	63.5	18.2	10.5	.28	.752	020		
ODD		3.54		3.7		3.66	3.1			3.72	3.1	.047	.953	012
CD		3.45		2.6		2.72	2.2			3.02	2.4	1.24	.291	201

CNR1 (Cannabinoid 1 receptor) (Dawson 1995)^c

ADHD	10.6	19.35	10.9	44.7	18.25	11.0	44.7	18.13	10.9	.174	.83	200		
ODD		4.67		3.1		3.54	3.1			3.56	3.2	1.89	.15	200
CD		3.09		2.2		2.90	2.3			3.03	2.4	.146	.86	202

CHRNA4 (Cholinergic, nicotinic, alpha 4) (Weiland, Steinlein 1996)^d

ADHD	8.0	22.19	9.2	36.2	18.90	10.8	55.8	17.19	11.2	2.35	.096	210		
ODD		5.07	3.0		3.59	3.0				3.55	3.2	2.74	.065	200
CD		3.11	2.1		2.93	2.3				2.99	2.4	.071	.930	200

NMDAR1 (Rupp et al. 1997) *Hpa* II SNP

ADHD	44.2	17.31	10.7	45.7	19.31	11.0	10.1	18.56	11.3	1.19	.303	021
ODD		3.79*	3.1		3.79*	3.1		4.84	3.1	2.93	.054	002
CD		2.83	2.3		3.07	2.3		3.28	2.7	.649	.523	012

ADORA2A (adenosine 2A receptor) (Deckert et al. 1996) C 108 T *Rsa* I.

ADHD	33.2	19.95	10.4	44.7	17.57	11.0	22.0	18.97	10.8	1.48	.229	201
ODD		4.04	3.3		3.41	3.1		4.02	3.1	1.52	.219	202
CD		3.39	2.5		2.82	2.1		2.83	2.4	2.04	.131	200

GRIN2B (glutamate ionotropic, NMDA 2B receptor) T/G (SNP database WIAF-1189).

ADHD	20.9	17.94	10.6	52.3	19.35	10.6	26.8	18.10	11.1	.582	.559	021
ODD		3.03*	3.0		4.15	3.1		3.50	3.1	3.22	.041	021
CD		2.36*	2.0		3.28	2.4		2.98	2.3	3.59	.029	021

NOS3 (nitric oxide synthase 3) (Wang et al. 1996)

ADHD	67.5	18.50	10.9	25.0	18.60	10.6	7.5	17.12	11.6	.186	.830	220
ODD		3.72	3.1		3.87	3.3		3.29	3.1	.311	.733	120
CD		3.00	2.3		3.12	2.2		2.33	1.9	1.08	.339	120

Opioids

PENK (proenkephalin) (Weber, May 1990; Comings et al. 1999a)^e

ADHD	32.1	18.71	10.4	47.4	18.02	11.3	20.6	18.25	11.0	.053	.948	201
ODD		3.75	3.2		3.75	3.2		3.48	3.1	.255	.775	220
CD		3.03	2.4		3.00	2.4		2.92	2.2	.041	.959	220

MME (enkephalinase) (see Methods) ^f

ADHD	33.9	19.44	11.0	50.9	17.34	10.9	15.2	19.53	10.9	1.26	.284	202	
ODD		3.98		3.25		3.44	3.1		3.95	3.0	1.00	.369	202
CD		3.10		2.4		2.81	2.3		3.32	2.4	1.08	.340	202

ANPEP (aminopeptidase N) (Watt, Willard 1990) and see Methods, A 257 G

ADHD	27.7	19.25	10.7	51.6	18.37	10.9	20.8	17.60	11.4	.398	.672	210	
ODD		3.65		3.1		3.95	3.1		3.30	3.2	.945	.389	120
CD		3.12		2.4		3.05	2.4		2.42	2.0	1.96	.142	210

NAT1 (N-acetyl transferase) T 1088 A (Dietz et al. 1997; Comings et al. 2000)

ADHD	5.7	21.50	9.5	34.7	19.00	11.2	59.6	17.86	10.8	1.11	.329	210	
ODD		4.94		3.7		3.51	3.2		3.68	3.1	1.58	.207	200
CD		4.11		2.8		3.00	2.3		2.88	2.2	2.26	.106	210

Hormones and neuropeptides

ESR1 (estrogen 1 receptor) dinucleotide repeat (del Senno et al. 1992; Comings et al. 1999).

ADHD	27.3	19.08	12.0	41.2	17.52	10.6	31.5	18.90	10.3	.673	.511	201	
ODD		3.82		3.4		3.56	3.0		3.86	3.0	.293	.746	202
CD		3.26		2.6		2.53*	2.0		3.33	2.5	4.09	.017	202

CYP19 (aromatase cytochrome P-450) dinucleotide repeat (Polymeropoulos et al. 1991b)^g

ADHD	13.4	16.88	11.6	45.2	17.28	11.7	41.4	19.76	9.9	2.11	.122	012	
ODD		3.50		3.1		3.33	3.0		4.11	3.3	2.16	.116	102
CD		3.07		2.4		2.52*	2.2		3.37	2.4	4.61	.011	102

SHBP (sex hormone binding protein) (Xu,Li 1998)

ADHD	59.8	18.39	11.2	35.2	18.38	10.4	5.0	17.44	11.4	.057	.944	220	
ODD		3.61		3.1		3.76	3.1		3.50	3.1	.108	.897	120
CD		2.85		2.3		3.11	2.3		3.06	1.8	.465	.628	021

CRH (corticosteroid releasing hormone) (*Xmn* I, Genome Database)

ADHD	89.8	18.25	11.1	8.6	18.78	8.8	1.5	25.00	7.9	1.189	.285	012	
ODD		3.66		3.2		3.71	2.8		5.60	3.2	.972	.380	012
CD		2.96		2.4		3.10	2.1		3.80	3.3	.370	.691	012

OXTR (oxytocin receptor) (Liao et al. 1996) silent C->T in exon 3

ADHD	47.1	18.48	10.5	44.3	18.0	11.5		8.7	20.11	10.7	.431	.650	102
ODD		3.59		3.1		3.65	3.2		4.39	2.8	.776	.461	012
CD		2.77		2.3		3.14	2.3		3.14	2.4	1.06	.347	022

CCK C-45 T (Ishiguro et al. 1999)

ADHD	77.0	18.57	10.8	20.4	17.66	11.0	2.2	19.71	14.3	.227	.797	102	
ODD		3.83		3.2		3.30	2.9		3.00	3.0	.909	.404	210
CD		3.04		2.4		2.71	2.2		3.14	2.3	.555	.574	102

INS (Hoban,Kelsey 1991; Gade-Andavolu et al. 1999)

ADHD	58.6	18.04	10.8	36.7	18.47	11.1	4.7	19.46	11.2	.147	.863	012	
ODD		3.68		3.2		3.70	3.1		3.66	3.6	.0014	.998	120
CD		2.95		2.3		2.98	2.4		3.47	1.6	.334	.716	002

CD8 (Polymeropoulos et al. 1991a)^h

ADHD	23.2	17.5	11.3	44.3	18.54	10.9	32.5	18.42	10.9	.122	.885	021	
ODD		3.31		3.2		4.09	3.2		3.44	3.0	1.95	.143	021
CD		2.53		2.1		3.27	2.5		2.92	2.1	2.44	.088	021

INFG (Wu,Comings 1998)

ADHD	21.8	18.22	10.9	58.3	18.17	10.9	27.9	18.82	10.8	.109	.896	102
ODD		3.78	2.97		3.69	3.2		3.60	3.2	.068	.934	210
CD		3.11	2.4		3.01	2.4		2.82	2.0	.333	.717	210

PSI (Scott et al. 1996)

ADHD	36.0	17.78	11.1	48.0	18.56	10.6	15.2	18.19	11.6	.215	.806	021
ODD		3.44	3.3		3.92	3.1		3.57	3.1	.828	.438	021
CD		2.59	2.1		3.18	2.4		3.30	2.5	2.68	.069	012

* Significantly lower than highest value by tukey test at $\alpha = .05$.

^a 11 = <188/<188, 12 = het. 22 ==188/=188

^b 11 ==10/=10, 12 = het. 22 =>10/>10

^c 11 = <5/<5 12 = het. 22 ==5/=5

^d 11 ==131/=131 12 = het. 22 =>131/>131

^e 11 ==178/=178 12 = het. 22 =>178/>178

^f 11 = a-c/a-c 12 = het. 22 = d-g/d-g

^g 11 = <4/<4 12 = het. 22 ==4/=4

^h 11 = 145/145 12 = 145/x 22 = x/x

Final Results for the 42 Genes for the ADHD, ODD and CD traits

Trait	r	r ²	adjusted r ²	F	p	# genes
ADHD	.466	.217	.16	3.82	<.0001	22
ODD	.443	.196	.14	3.58	<.0001	20
CD	.451	.203	.15	3.94	<.0001	19

Figure 2

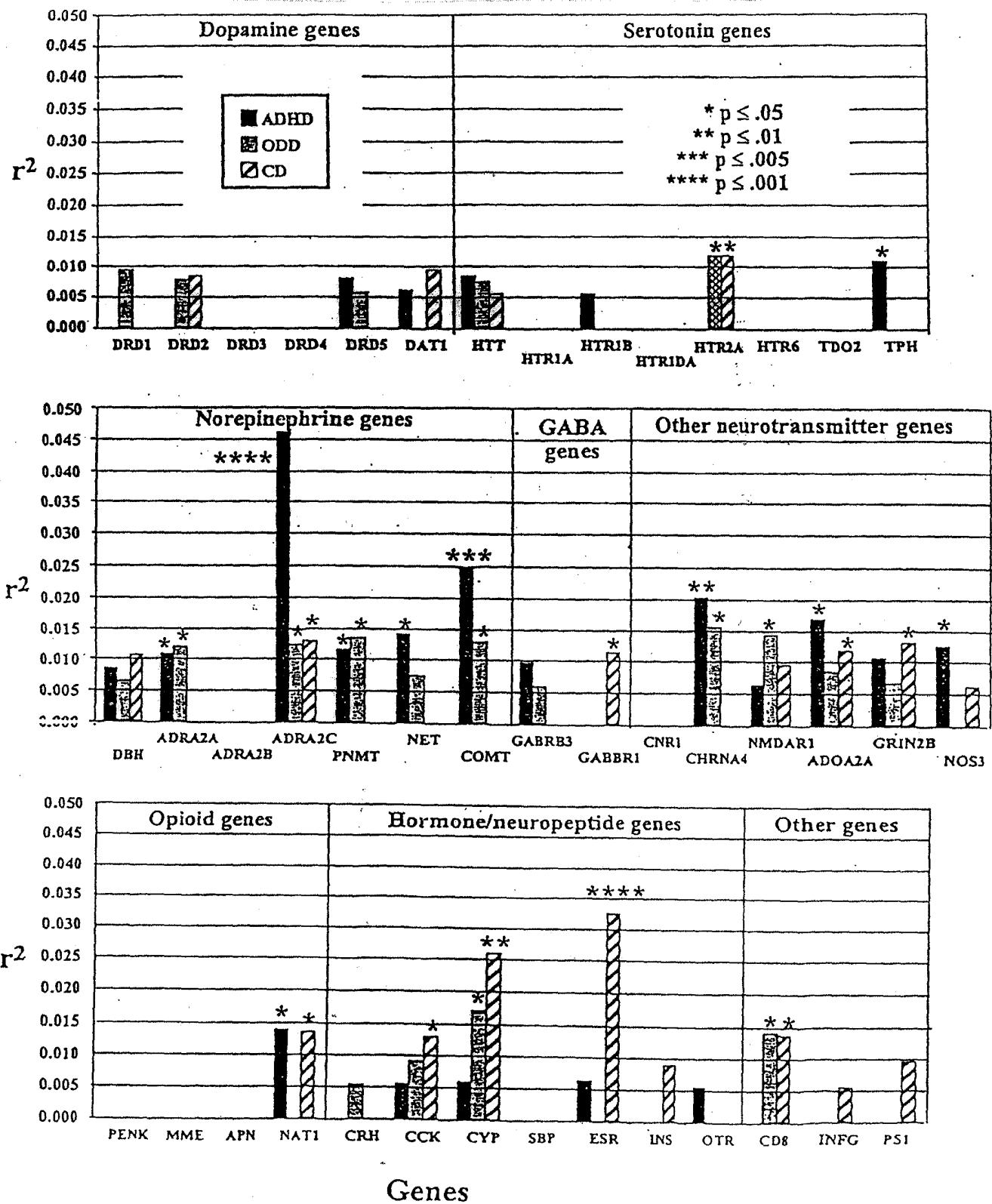


Figure 3

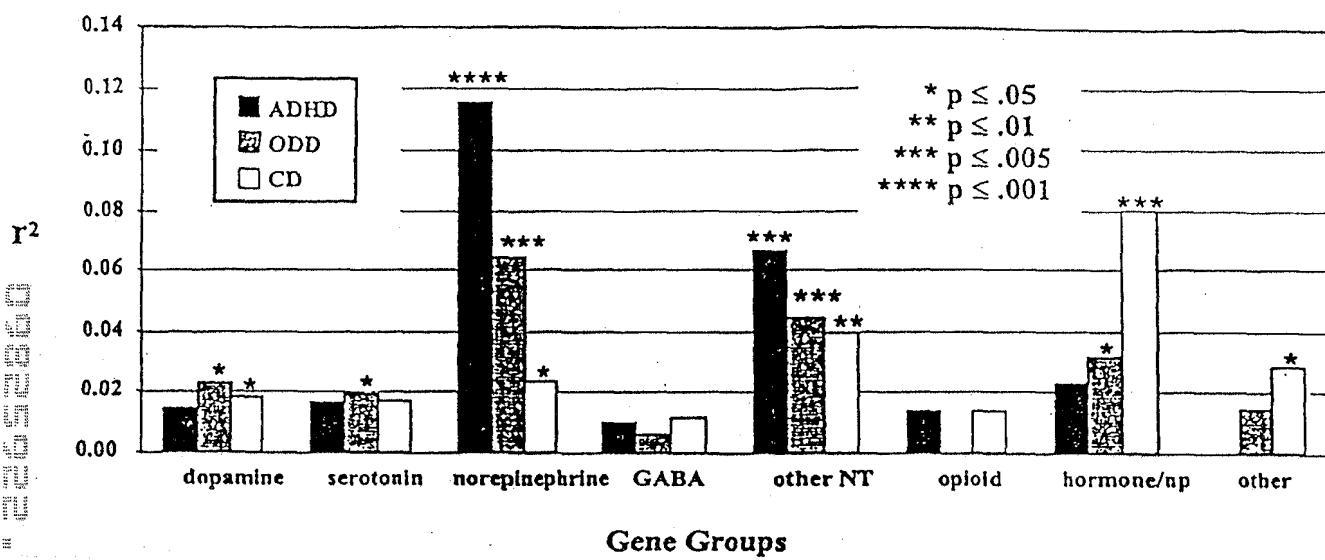


FIGURE 4